

Insights into Release of Interleukin-1 β from Platelets

Tobias Geisler¹

¹Department of Cardiology and Angiology, Eberhard Karls University Tübingen Faculty of Medicine, Tübingen, Baden-Württemberg, Germany

Thromb Haemost 2022;122:475.

Address for correspondence Tobias Geisler, MD, Department of Cardiology and Angiology, Eberhard Karls University Tübingen Faculty of Medicine, Otfried-Müller-Strasse 10, Tübingen, Baden-Württemberg 72076, Germany
(e-mail: tobias.geisler@med.uni-tuebingen.de; togeisler@web.de).

Platelets are key players in the crosstalk between inflammation and thrombosis. Therefore, insights that elucidate the mechanisms of platelet-dependent thromboinflammation are of high interest. Interleukin 1 β (IL-1 β) is mainly involved in NLRP3 inflammasome complex formation. IL-1 β has been found to be an attractive target to suppress chronic vascular inflammation, thus improving prognosis in atherosclerotic disease.¹ Although controversial data exist, it has been proposed that resting platelets contain relevant amounts of preformed IL-1 β . Besides their effects on inflammatory cells, IL-1 receptor and IL-1 β play a role in megakaryocyte maturation and platelet activation.² The work by Pennings et al published in this issue adds to the current knowledge by shedding light on the mechanism of IL-1 β release from platelets.³ The authors convincingly demonstrated that preformed IL-1 β protein can be released shortly within minutes after activation of platelets by ADP, protease-activated receptor (PAR)1, and PAR4-activating peptides. The process of IL-1 β significantly correlated with the degree of platelet activation. Release of IL-1 β was independent of extracellular NLRP3 activation as indicated by missing signals on NLRP3 expression/phosphorylation and caspase-1 activation. Still, it is unclear based on the performed ELISA experiments whether the protein is pro-IL-1 β or mature-IL-1 β and whether NLRP3 or caspase-1 is involved in the formation of intracellular pro-IL-1 β . Although repeatedly demonstrated that platelets despite being anucleate are capable of de-novo protein synthesis, the question about the source of intraplatelet IL-1 β is still a matter of debate. The potential translational aspects of the findings warrant further investigation. Besides the role of IL-1 β inflammasome activation for

leukocyte production and recruitment in atherosclerosis,⁴ what is the function of inflammasome-independent platelet IL-1 β ? Are the detected concentrations high enough to convey substantial cellular signals and to promote alterations in the vascular environment? Experiments in mouse models indicate that IL-1 β can induce thrombocytosis, suggesting that platelets could support an inflammatory feedback loop by amplifying IL-1 signaling and triggering platelet biogenesis.⁵ Whether platelet-derived IL-1 β contributes to this loop in the human system and what clinical impact targeting platelet IL-1 β might have require deeper insight.

Conflict of Interest

None declared.

References

- 1 Ridker PM, Everett BM, Thuren T, et al; CANTOS Trial Group. Antiinflammatory therapy with canakinumab for atherosclerotic disease. *N Engl J Med* 2017;377(12):1119–1131
- 2 Beaulieu LM, Lin E, Mick E, et al. Interleukin 1 receptor 1 and interleukin 1 β regulate megakaryocyte maturation, platelet activation, and transcript profile during inflammation in mice and humans. *Arterioscler Thromb Vasc Biol* 2014;34(03):552–564
- 3 Pennings GJ, Reddel CJ, Traini M, et al. Rapid release of interleukin-1 β from human platelets is independent of NLRP3 and caspase. *Thromb Haemost* 2022;122(4):517–528
- 4 Hettwer J, Hinterdobler J, Miritsch B, et al. Interleukin-1 β suppression dampens inflammatory leukocyte production and uptake in atherosclerosis. *Cardiovasc Res* 2021. Doi: 10.1093/cvr/cvab337
- 5 Kimura H, Ishibashi T, Shikama Y, et al. Interleukin-1 beta (IL-1 beta) induces thrombocytosis in mice: possible implication of IL-6. *Blood* 1990;76(12):2493–2500

received

October 27, 2021

accepted

October 28, 2021

published online

November 1, 2021

© 2021. Thieme. All rights reserved.

Georg Thieme Verlag KG,

Rüdigerstraße 14,

70469 Stuttgart, Germany

DOI <https://doi.org/10.1055/a-1683-8567>.

ISSN 0340-6245.